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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/652,282	08/30/2000	Maurice Kent Gately	9483	2369

7590 12/31/2003

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EXAMINER
ROARK, JESSICA H

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/652,282	GATELY ET AL.	
	Examiner	Art Unit	
	Jessica H. Roark	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15-20 and 37-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-20 and 37-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. The Examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Jessica Roark, Art Unit 1644, Technology Center 1600.

2. *Claims* 15-20 and 37-40 *are pending and under consideration in the instant application.*

3. This Office Action will be in response to applicant's arguments, filed 10/6/03 .
The rejections of record can be found in the previous Office Action.

35 USC § 112

4. Applicant's arguments, filed 10/6/03 regarding the art-recognized definition of the term "immunologically reactive" is found convincing. The previous rejection of claims 15-20 and 37-40 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention

Claim Rejections – 35 U.S.C. §§ 102 and 103

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless --

> *(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.*

6. Claims 15-17, 19-20, 37 and 39 stand rejected under 35 U.S.C. 102(e) as being anticipated by Trinchieri et al. (5,811,523, of record), as evidenced by Gately et al. (US Patent 5,780,597, of record) and Carter et al (IDS reference 16) and Colman (Res Immunol. 1994 Jan;145(1):33-6, of record).

Applicant's arguments, filed 10/6/03, have been fully considered but have not been found convincing for the reasons of record.

The rejection of record is re-iterated below:

The instant claims are drawn to a monoclonal antibody to human IL-12 which consists of a p35 subunit and a p40 subunit forming a p75 heterodimer, wherein said monoclonal antibody immunologically reacts with an epitope presented by the p75 heterodimer of human IL-12, but is not immunologically reactive with any epitope presented by said p40 subunit.

'523 teaches a polyclonal and monoclonal antibody which reacts with the human cytokine NKSF heterodimer (which appears to have the same sequence as IL-12 as evidenced by Gately et al.) and is specific for the 35KD subunit which has the same sequence as the sequence of the IL-12 35KD subunit, (see entire patent, especially column 10, lines 25-28, claims 1, 3-5 and 7 and Figures 1-2). Specifically, claim 1 of '523 teaches that said antibody specifically reacts with the heterodimer, and claim 3 of '523 which depends from claim 1, teaches that said antibody reacts with the p35 subunit.

'523 reads on the limitation that said antibody is not immunologically reactive with any epitope presented by said p40 subunit, because said referenced antibody, which immunologically reacts with the p35 subunit, would not immunologically react with the p40 subunit because the amino acid sequences of the two subunits are distinct and because antibody recognition is sequence dependent, as evidenced by Colman. Colman teaches that even single amino acid changes in the antigen can effectively abolish the antibody antigen interaction entirely (see entire article, including page 33, second column).

With regard to the properties of the antibodies recited in the instant claims, i.e. the concentrations of antibody and human IL-12 and by "inhibiting IL-12 stimulated PHA activated human lymphoblast proliferation" and "by inhibiting IL-12 stimulated IFN-γ production", the referenced antibody has the specificity of the claimed antibody, and the functional properties are considered inherent properties of the referenced antibody. The claimed antibody appears to be the same as the referenced antibody, absent a showing of any differences. Since the Patent Office does not have the facilities for comparing the antibody of the instant invention to those of the prior art, the burden is on the applicant to show an unobvious distinction between the molecule of the instant invention and that of the prior art, see *In re Best*, 562 F.2d 152, 195 USPQ 430 (CCPA 1977).

With regard to the recited limitation of the antibody having cross reactivity with rhesus monkey IL-12, it is an inherent property of said recited anti-human IL-12 antibody that it would cross react with rhesus monkey IL-12 to some extent as evidenced by Carter et al who teach cross-reactivity of antibodies to IL-12 with mouse Il-12 and human IL-12 (about 60%, see especially page 367, second column, lines 6-8) and the degree of homology between human and mouse Il-12 is less than the homology between human and rhesus Il-12.

With regard to the recited limitation that the antibody is produced by a hybridoma, said production is encompassed by '523's teaching that the referenced monoclonal antibodies can be made by standard methods, which includes hybridoma technology.

Applicant's Arguments and Response:

Applicant argues that the antibody taught by the '523 patent does not necessarily neutralize at least about 90% of the bioactivities of IL-12 as required by the claims and that the antibody of the '523 patent therefore fails to anticipate the instant claims. For support for this argument, Applicant notes that the 20C2 antibody is disclosed in the specification as filed to be an antibody that binds the p75 heterodimer of IL-12, but does not react with either the p35 or p40 subunit alone (Remarks filed 10/6/03, page 5). Applicant points out that the specification discloses that the 20C2 antibody does not have the ability to neutralize at least about 90% of the bioactivity of IL-12 as required by the claims. Applicant concludes that because the 20C2 antibody does not possess the functional activity required by the instant claims, the antibody taught by the '523 patent does not necessarily possess the recited function.

The Examiner acknowledges that the 20C2 antibody is an anti-IL12 antibody that does not possess the functional activities required by the instant claims. However, there is an important difference between the 20C2 antibody and the antibody taught and claimed by the '523 patent: the 20C2 antibody binds the p75 heterodimer does not bind the p35 subunit of IL-12, whereas the antibody claimed in the '523 patent binds both the p75 heterodimer (e.g., claim 1) and binds the p35 subunit (e.g., claim 3). Thus Applicant has not established that an antibody with the same binding specificity as that set forth in the '523 patent does not necessarily possess the recited properties.

The rejection is therefore maintained for the reasons of record.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 15, 16, 18 and 38-40 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Trinchieri et al. (5,811,523, of record), in view of Gately et al. (US Patent 5,780,597, of record), Carter et al (IDS reference 16), Colman (Res Immunol. 1994 Jan;145(1):33-6, of record) and Bendig (Methods: A Companion to Methods in Enzymology Vol. 8:83-93, 1995, of record).

Applicant's arguments, filed 10/6/03, have been fully considered but have not been found convincing for the reasons of record.

The rejection of record is re-iterated below:

> As previously noted, Trinchieri et al. (5,811,523), Gately et al., Carter et al and Colman teach as discussed supra, but do not teach that the antibody is humanized.
>
> Trinchieri et al. (5,811,523) further teaches that said antibodies can be used for therapeutic uses, and that NKSF (or IL-12) stimulates NK cells and IFN-γ production by PBL, (see entire patent, especially column 21, lines 14-19).
>
> Bendig teaches that clinical results with rodent antibodies have been disappointing primarily because rodent antibodies are highly immunogenic in humans. Bendig further teaches that to help overcome this problem, rodent antibodies have been humanized, and teaches that reliable methods for humanization have been developed.
>
> The Examiner maintains that it would therefore have been obvious to one of skill in the art, who wanted to use the antibodies taught by '523 for in vivo therapy for humans, to have humanized the antibody taught by '523 made in rodents because Bendig teaches that the problem of immunogenicity of rodent antibodies in humans has been alleviated by humanizing rodent antibodies and because '523 teaches therapeutic uses for said antibodies directed against NKSF (IL-12). One would have an expectation of success because Bendig also teaches that reliable methods for humanization have been developed.
>
> From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Applicant's Arguments and Response:

Applicant argues that for the reasons addressed with respect to the rejection under 35 U.S.C. 102(e), the antibody taught and claimed in the '523 patent also does not teach or suggest the antibody of claims 15, 16, 18 and 38-40, and that the teachings of the other cited references do not remedy this defect.

Applicant's argument has been addressed supra. No additional arguments are advanced regarding the obviousness of humanizing an antibody taught by the prior art.

The rejection is therefore maintained for the reasons of record.

Conclusion

9. No claim is allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209 (effective mid January 2004, this number will change to (571) 272-0848). The examiner can normally be reached Monday from 8:30 to 5:00, and Tuesday/Thursday from 10:00 to 4:00. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number for before Final submissions is (703) 872-9306.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
December 18, 2003

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
12/22/03